

Postdated versus usual delayed antibiotic prescriptions in primary care

Reduction in antibiotic use for acute respiratory infections?

Graham Worrall MD MSc MBBS FCFP Angela Kettle RN Wendy Graham MD CCFP FCFP Jim Hutchinson MD

ABSTRACT

OBJECTIVE To determine whether postdating delayed antibiotic prescriptions results in a further decrease (over usual delayed prescriptions) in antibiotic use.

DESIGN Randomized controlled trial.

SETTING A small rural town in Newfoundland and Labrador.

PARTICIPANTS A total of 149 consecutive adult primary care patients who presented with acute upper respiratory tract infections.

INTERVENTION Delayed prescriptions for patients who might require antibiotics were randomly dated either the day of the office visit (ie, the usual group) or 2 days later (ie, the postdated group).

MAIN OUTCOME MEASURES Whether or not the prescriptions were filled and the time it took for the patients to fill the prescriptions were noted by the 4 local pharmacies and relayed to the investigators.

RESULTS In total, 149 delayed antibiotic prescriptions were written, 1 per patient. Of the 74 usual delayed prescriptions given out, 32 (43.2%) were filled; of the 75 postdated delayed prescriptions given out, 33 (44.0%) were filled. Sixteen patients from each group filled their delayed prescriptions earlier than the recommended 48 hours. Statistical analyses— χ^2 tests to compare the rates of antibiotic use between the 2 groups and t tests to compare the mean time to fill the prescription between the 2 groups—indicated that these results were not significant ($P > .05$).

CONCLUSION Although delayed prescriptions reduce the rate of antibiotic use, postdating the delayed prescription does not seem to lead to further reduction in use.

EDITOR'S KEY POINTS

- Inappropriate prescribing of antibiotics for conditions caused by viral infections is widespread and is a contributing factor to antibiotic overuse leading to resistance; however, previous studies have shown that delayed prescribing practices can reduce antibiotic consumption.
- *Delayed prescribing* refers to the process of issuing a prescription for a condition that might have a bacterial cause (but likely not) and instructing the patient to wait a certain amount of time before filling it; should the condition worsen or stay the same after that time, the prescription can be filled. In the interim, the patients are advised to treat the symptoms with over-the-counter remedies for overall relief.
- This study aimed to ascertain whether providing postdated delayed prescriptions would be even more effective in reducing antibiotic consumption compared with delayed prescriptions dated the day of the office visit. Although there was no significant difference in antibiotic use between the usual and postdated delayed prescription groups, the authors confirmed that patients do not rush to fill delayed prescriptions for antibiotics.
- In order to avoid unnecessary antibiotic consumption, further trials focusing on clinician rather than patient habits will be conducted to evaluate intervention methods for reducing inappropriate antibiotic prescribing in family practice.



This article is eligible for Mainpro-M1 credits. To earn credits, go to www.cfp.ca and click on the Mainpro link.

This article has been peer reviewed.
Can Fam Physician 2010;56:1032-6

Dans les soins primaires, la prescription différée d'antibiotiques habituelle ou postdatée?

Réduction du recours aux antibiotiques contre les infections respiratoires aiguës

Graham Worrall MD MSc MBBS FCFP Angela Kettle RN Wendy Graham MD CCFP FCFP Jim Hutchinson MD

RÉSUMÉ

OBJECTIF Déterminer si le fait de postdater les prescriptions d'antibiotiques différées entraîne une plus grande réduction de l'utilisation des antibiotiques que les prescriptions différées habituelles..

TYPE D'ÉTUDE Essai randomisé avec témoins.

CONTEXTE Une petite localité rurale de Terre-Neuve et Labrador.

PARTICIPANTS Un total de 149 patients adultes consécutifs en médecine primaire consultant pour une infection des voies respiratoires aiguës.

INTERVENTION De façon aléatoire, les prescriptions différées pour les patients susceptibles de nécessiter ultérieurement des antibiotiques ont été préparées en date de la journée de la consultation (i. e. mode habituel) ou pour 2 jours plus tard (groupe postdaté).

PRINCIPAUX PARAMÈTRES MESURÉS Les 4 pharmacies locales ont noté si les prescriptions ont été remplies ou non, et le temps qu'il a fallu aux patients pour les faire remplir. Ces renseignements ont été transmis aux chercheurs.

RÉSULTATS On a fait un total de 149 prescriptions différées d'antibiotiques, une par patient. Sur les 74 prescriptions différées habituelles, 32 (43,2%) ont été remplies; sur les 75 prescriptions différées postdatées, 33 (44%) ont été remplies. Seize patients de chacun des groupes ont fait remplir leur prescription avant le délai recommandé de 48 heures. L'analyse statistique – comparaison par tests de χ^2 des taux d'utilisation d'antibiotiques entre les 2 groupes et par tests de t pour les moyennes des délais pour remplir les prescriptions – indiquait que ces résultats n'étaient pas significatifs ($P > .05$).

CONCLUSION Même si les prescriptions différées diminuent le taux de consommation d'antibiotiques, le fait de postdater ces prescriptions ne semble pas diminuer davantage cette utilisation.

POINTS DE REPÈRE DU RÉDACTEUR

- On prescrit souvent (et à tort) des antibiotiques pour des infections d'origine virale, contribuant ainsi à une utilisation excessive des antibiotiques et à une augmentation de la résistance; des études antérieures ont toutefois montré qu'une prescription différée (à remplir plus tard) peut diminuer la consommation d'antibiotiques.
- Une prescription différée est une prescription pour une infection possiblement (mais peu probablement) bactérienne, le patient étant alors avisé d'attendre un certain temps avant de la faire remplir; toutefois, si la condition empire ou ne s'améliore pas après ce délai, la prescription peut être remplie. Entre temps, on conseille au patient de traiter les symptômes avec des remèdes en vente libre.
- Cette étude voulait déterminer si les prescriptions différées postdatées seraient plus efficaces que celles datées du jour de la consultation pour réduire la consommation d'antibiotiques. Même s'il n'y avait pas de différence significative dans l'utilisation des antibiotiques entre le groupe avec prescription différée habituelle et celui avec prescription postdatée, les auteurs ont confirmé que les patients ne se précipitent pas pour remplir leur prescription différée d'antibiotiques.
- D'autres études axées sur les habitudes des médecins plutôt que sur celles des patients seront nécessaires pour évaluer les modes d'intervention susceptibles de réduire la prescription inappropriée des antibiotiques en médecine familiale.



Cet article donne droit à des crédits Mainpro-M1. Pour obtenir des crédits, allez à www.cfp.ca et cliquez sur le lien vers Mainpro.

Cet article a fait l'objet d'une révision par des pairs.
Can Fam Physician 2010;56:1032-6

Inappropriate prescribing of antibiotics for acute respiratory tract infections (which are usually caused by viruses) is widespread.¹⁻³ It is well known that inappropriate overuse of antibiotics is partly responsible for antibiotic resistance.⁴ Family doctors are aware that antibiotics are not much use for patients with these infections, yet many continue to prescribe them “against the evidence.”⁵⁻⁷

Some family doctors have adopted the use of delayed antibiotic prescriptions for common respiratory infections. A delayed prescription is given to the patient at the time of the office visit and can be filled and the antibiotics used if the illness symptoms do not improve within a mutually agreed upon time—usually about 48 hours. The first evidence on the benefits of delayed prescriptions came from a randomized controlled trial published in 1997, in which Little and his colleagues in Southampton, England, found that antibiotic prescriptions with a 3-day delay period for patients with acute sore throat reduced the number of patients actually taking the antibiotics from 99% to 31%.⁸ Since then there have been 6 other trials on the use of delayed prescriptions, all of which have shown reduction in antibiotic use.⁹⁻¹⁴

There is, therefore, strong evidence that the use of delayed antibiotic prescriptions results in a large drop in antibiotic use. We wondered whether postdating the prescription so that the patient was, in theory, unable to use it immediately might cause a further reduction in antibiotic use. We designed a trial to compare the antibiotic prescription uptake rates of delayed prescriptions that could be filled immediately with the uptake rates of postdated prescriptions that could only be used after a certain time. As nurse practitioners (NPs) are now commonly the first point of contact in acute primary care, we involved them as well as FPs in our study.

METHODS

This was a randomized controlled trial, approved by Memorial University of Newfoundland’s Human Investigations Committee (No. 06.049).

Six FPs and 2 NPs in a small community in Newfoundland and Labrador were asked to recruit consecutive adult patients (aged 18 years or older) with acute upper respiratory tract infections for whom the clinicians thought antibiotic treatment might not be necessary. After a standardized explanation of the likely viral, benign, and self-limiting nature of the illness (**Box 1**), the patient was randomly given a delayed prescription dated for either the day of the office visit (ie, the *usual* prescription), or 2 days later (ie, the *postdated* prescription). In each case the patient was asked to use the prescription only if symptoms had not improved or had worsened after 2 days. Clinicians were asked to follow their usual practices

Box 1. Script for physicians and nurses when issuing delayed antibiotic prescriptions

I think you are suffering from [provide diagnosis]. This condition is usually caused by a virus and tends to get better by itself, without any curative treatment. All that should be necessary is treatment to relieve your symptoms—[insert suggestions]—and the illness will likely improve within a few days.

Although most infections are caused by viruses, and antibiotics do not help with recovery, a small number of infections like yours can be caused by bacteria; we treat these infections with antibiotics. Unfortunately, we cannot tell by examining you whether you have the usual virus-type infection or whether you are one of the few who have a bacterial infection. We now prescribe fewer antibiotics than we used to, not only because they don't cure most infections like yours, but because they can cause unpleasant side effects like diarrhea, vomiting, and skin rashes.

Here is what I suggest: I shall give you a prescription for an antibiotic. I think that you should not fill this prescription now, but wait for 2 days to see how your illness progresses. If, after 2 days, your symptoms are getting worse or there is no improvement, you can take the prescription to the pharmacist and start taking the antibiotic. If, at any time, new symptoms develop, or you are worried about your illness, you can call me or come to see me again.

Do you have questions about what we are doing?

regarding symptomatic treatment. Patients with concerns were asked to call their respective clinicians.

Randomization

When the clinician had determined whether a patient was eligible for the study, a blank envelope containing either a usual or a postdated delayed prescription was opened in front of the patient. By block randomization, each FP and NP was given an equal number of both prescriptions.

Prescriptions and pharmacists

The delayed prescriptions were on specially marked pads so that they could easily be identified by local pharmacists. All 4 pharmacies in the study area took part. It was unlikely participants went to a pharmacy outside the study area, as the next closest town was 200 km away. During the period of the study, the pharmacies were regularly contacted by the research assistant to determine how many study prescriptions had been filled and on what date each prescription was filled. If a patient filled a delayed prescription before the due date, the pharmacist was asked to note in a logbook the reason given by the patient.

Statistical analysis

Our null hypothesis was that there would be no difference in antibiotic prescription consumption rates

between the usual and postdated delayed prescription groups. If the usual prescription uptake is 85%, a sample size of 150 (75 in each arm of the study) is sufficient to detect a 20% difference in rates (which we judged to be clinically significant) at $\alpha = .05$ and $\beta = .2$.¹⁵ Proportions were compared using the χ^2 test, and means were compared using the t test.

RESULTS

Six FPs and 2 NPs took part in the study. **Table 1** shows the patients' conditions as diagnosed by the clinicians writing the delayed antibiotic prescriptions. The most common condition was upper respiratory tract infection, followed by sinusitis, bronchitis, and pharyngitis. The range of illnesses was similar in both the usual and the postdated groups.

Table 1. Diagnoses made by clinicians who issued delayed prescriptions

DIAGNOSIS	USUAL PRESCRIPTION*	POSTDATED PRESCRIPTION†	TOTAL
URTI	25	20	45
Sinusitis	11	19	30
Bronchitis	15	10	25
Pharyngitis	12	13	25
Acute otitis media	7	12	19
Soft tissue infection	2	0	2
Laryngitis	1	1	2
CAP	1	0	1
Total	74	75	149

CAP—community-acquired pneumonia, URTI—upper-respiratory tract infection.

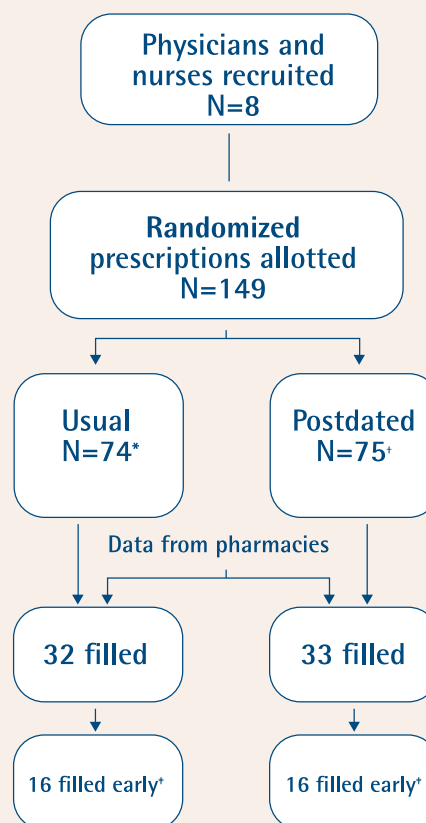
*Usual prescription refers to prescriptions that were dated the day of the office visit, despite a recommended delay in filling the prescription of 48 hours.

†Postdated prescription refers to prescriptions postdated 48 hours after the office visit.

The clinicians wrote 149 delayed antibiotic prescriptions, of which 74 were usual and 75 were postdated. In total, 65 of 149 prescriptions were filled (43.6%): 32 (43.2%) usual prescriptions and 33 (44.0%) postdated prescriptions (not significant [NS]; $\chi^2 = 0.009$, $P = .924$). **Figure 1** represents a flow chart of the design and outcomes of the trial.

Of the 65 prescriptions filled, 32 were filled within 2 days of being written—16 usual and 16 postdated (NS; $\chi^2 = 0.001$, $P = .975$). The time it took to fill the other 33 prescriptions ranged from 3 to 19 days, with a mean of 6.1 days in the usual group and a mean of 6.5 days in the postdated group (NS; $t = 0.041$, $P = .968$).

Figure 1. Flowchart depicting the study design and outcomes



*Usual prescriptions refer to prescriptions that are dated the day of the office visit, despite a recommended delay in filling the prescription of 48 hours.

†Postdated prescriptions refer to prescriptions postdated 48 hours after the office visit.

*Prescriptions that were filled within 2 days, during the period of delay.

Table 2. Reasons provided by patients when asking for delayed prescriptions to be filled early: N=32.

REASON	N*
Still unwell	15
Getting worse	6
Patient was adamant (no reason provided)	7
Leaving town	4
Did not want to see a doctor again	1
Will not get better without it	1
Long weekend	1
OTC medication suggested by FP not available	1

OTC—over the counter

*Total number equals more than 32, as some patients gave more than 1 reason.

Table 2 indicates the reasons given to the pharmacist by patients who filled their delayed prescriptions early (ie, within the 2-day delay period). The most common reason was that the patient was “unwell” or “getting

worse"; in 7 cases the patients were "adamant" that they wanted to fill the prescriptions immediately, and in 4 cases the patients were "leaving town."

DISCUSSION

We found, as did other studies,⁸⁻¹⁴ that issuing delayed prescriptions results in a large drop in antibiotic use. In our study, total antibiotic use was only 43%, more than necessary in the treatment of predominantly viral illnesses, but much lower than typical rates of antibiotic use in the developed world in general⁵⁻⁷ and in Newfoundland specifically.¹⁶ Other studies have found that delayed prescriptions result in rates of antibiotic use from 24%¹⁰ to 65%⁹; ours was in the middle of that range. We realize that a short study like this will not affect clinician prescribing habits; however, a British trial is currently evaluating a complex multifaceted intervention to reduce the rates of inappropriate antibiotic prescribing in general practice.¹⁷

An article from the Cochrane Database of Systematic Reviews, which looked at the effects of delayed antibiotics on symptoms and complications of respiratory infections, found that there was no difference for most symptom measures between using immediate and delayed antibiotics for symptoms on day 1 and day 7.¹⁸ Of the 6 studies that reported fever, 3 found increased fever in the delayed antibiotic group. Another study found that in children with acute otitis media, pain and malaise severity scores favoured the immediate prescription group.⁹ Overall, however, there was no danger in delaying antibiotic use.

We found that postdating the delayed antibiotic prescription had no effect on either the number of prescriptions filled or the time it took for patients to get their antibiotics from the pharmacist. Although both patients and pharmacists knew that postdated prescriptions should not be filled until their due date, equal proportions of usual and postdated delayed prescriptions were filled on the day of the office visit or the following day (in each group, about half of the patients who filled their prescriptions filled them earlier than the clinicians had suggested, for a variety of reasons).

Limitations

Both clinicians and patients knew they were participating in a study and might have been subject to the Hawthorne effect (ie, a form of reactivity in which people improve or modify an aspect of their behaviour when they know they are being studied). Also, the block randomization process gave clinicians an equal number of usual and postdated prescriptions; as they reached the end of their allotted prescriptions, clinicians might have known what the remaining prescriptions were, introducing possible bias.

Conclusion

We believe our study has confirmed that the use of delayed prescriptions results in a large drop in antibiotic use by adult patients with acute respiratory infections. We also think that physicians need not worry overmuch that patients will rush out and fill delayed prescriptions at once; it appears that only about 1 in 5 will do so, regardless of whether or not the prescription is postdated.

Dr Worrall is an Honorary Research Professor in the Department of Family Medicine at Memorial University of Newfoundland in St John's. **Ms Kettle** is a nurse and research assistant at the Charles Legrow Health Centre in Channel-Port aux Basques, Nfld. **Dr Graham** is a rural family physician in St John's and an Assistant Professor in the Department of Family Medicine at Memorial University of Newfoundland. **Dr Hutchinson** is an Associate Professor of Laboratory Medicine at Memorial University of Newfoundland.

Contributors

Dr Worrall, Ms Kettle, Dr Graham, and Dr Hutchinson all contributed to the concept and design of the study; data gathering, analysis, and interpretation; and preparing the manuscript for submission.

Competing interests

None declared

Correspondence

Dr Graham John Worrall, P.O. Box 241, Glovertown, NL A0G 2L0; telephone 709 533-2856; e-mail gworrall@mun.ca

References

- Macfarlane J, Lewis SA, Macfarlane R, Holmes W. Contemporary use of antibiotics in adults presenting with acute respiratory tract infection in general practice in the UK: implications for developing implementation guidelines. *Respir Med* 1997;91:427-33.
- Nyquist AC, Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for children with colds, upper respiratory tract infections, and bronchitis. *JAMA* 1998;279(11):875-7.
- Cars O, Mölsted S, Melander A. Variation in antibiotic use in the European Union. *Lancet* 2001;357(9271):1851-3.
- Gould IM. Antibiotic resistance: the perfect storm. *Int J Antimicrob Agents* 2009;34(Suppl 3):S2-5.
- McCaig LF, Hughes JM. Trends in antimicrobial drug prescribing among office-based physicians in the United States. *JAMA* 1995;273(3):2414-9. Erratum in: *JAMA* 1998;279(6):434.
- Cantrell R, Young AF, Martin BC. Antibiotic prescribing in ambulatory care settings for adults with colds, upper respiratory tract infections, and bronchitis. *Clin Ther* 2002;24(1):170-82.
- Watson RL, Dowell SF, Jayaraman M, Keyserling H, Kolczak M, Schwartz B. Antimicrobial use for pediatric upper respiratory infections: reported practice, actual practice, and parent beliefs. *Pediatrics* 1999;104(6):1251-7.
- Little P, Williamson I, Warner G, Gould C, Gantley M, Kinmonth AL. Open randomised trial of prescribing strategies in managing sore throat. *BMJ* 1997;314(7082):722-7.
- Cates C. An evidence based approach to reducing antibiotic use in children with acute otitis media: controlled before and after study. *BMJ* 1999;318(7185):715-6.
- Little P, Gould C, Williamson I, Moore M, Warner G, Dunleavy J. Pragmatic randomised controlled trial of two prescribing strategies for childhood acute otitis media. *BMJ* 2001;322(7282):336-42.
- Dowell J, Pitkethly M, Bain J, Martin S. A randomised controlled trial of delayed antibiotic prescribing as a strategy for managing uncomplicated respiratory tract infection in primary care. *Br J Gen Pract* 2001;51(464):200-5.
- Arroll B, Kenealy T, Kerse N. Do delayed prescriptions reduce the use of antibiotics for the common cold? A single-blind controlled trial. *J Fam Pract* 2002;51(4):324-8.
- Macfarlane J, Holmes W, Gard P, Thornhill D, Macfarlane R, Hubbard R. Reducing antibiotic use for acute bronchitis in primary care: blinded, randomised controlled trial of patient information leaflet. *BMJ* 2002;324(7329):91-4.
- Siegel RM, Kiely M, Bien JP, Joseph EC, Davis JB, Mendel SG, et al. Treatment of otitis media with observation and a safety-net antibiotic prescription. *Pediatrics* 2003;112(2 Pt 1):527-31.
- Sackett DL, Haynes RB, Guyatt GH, Tugwell P. *Clinical epidemiology: a basic science for clinical medicine*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 1991.
- Hutchinson JM, Foley RN. Method of physician remuneration and rates of antibiotic prescription. *CMAJ* 1999;160(7):1013-7.
- Simpson SA, Butler CC, Hood K, Cohen D, Dunstan F, Evans MR, et al. Stemming the Tide of Antibiotic Resistance (STAR): a protocol for a trial of a complex intervention addressing the 'why' and 'how' of appropriate antibiotic prescribing in general practice. *BMC Fam Pract* 2009;10:20.
- Spurling GK, Del Mar CB, Dooley L, Foxlee R. Delayed antibiotics for symptoms and complications of respiratory infections. *Cochrane Database Syst Rev* 2004;(4):CD004417.